

Exhibit A

HIGHLY CONFIDENTIAL PURSUANT TO PROTECTIVE ORDER

Transcript of Alexander Bridges, Ph.D.

Conducted on April 18, 2019

2

1 IN THE UNITED STATES DISTRICT COURT

2 NORTHERN DISTRICT CALIFORNIA

3 OAKLAND DIVISION

4 ---oOo---

5 PLEXXIKON INC.,

6 Plaintiff,

7 vs.

No. 4:17-cv-04405-HSG

8 NOVARTIS PHARMACEUTICALS
9 CORPORATION,

10 Defendant.
11 _____/

12
13
14 Videotaped Deposition of Alexander Bridges, Ph.D.,
15 taken on behalf of the Defendant, on Thursday,
16 April 18, 2019, at Durie Tangri, 217 Leidesdorff
17 Street, San Francisco, California, beginning
18 9:08 a.m., and commencing at 12:15 p.m., Pursuant
19 to Notice, and before me, ANDREA M. IGNACIO, CSR,
20 RPR, CRR, CLR ~ License No. 9830.
21
22
23
24
25

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1 problems.

09:14:41

2 A lot of the time, I'm more employed for my
3 medicinal chemistry expertise, which is not actually
4 involved in the synthesis, and in my sort of
5 peripheral knowledge of biology and general experience
6 in the industry.

09:14:41

09:14:44

09:14:48

09:14:51

09:14:56

7 Q But from time to time in your role as a
8 consultant, you get called upon to help companies
9 design ways to synthesize molecules; right?

09:15:03

09:15:06

09:15:10

10 A That is correct, yes.

09:15:14

11 Q Would you consider yourself an expert in the
12 Suzuki reaction?

09:15:15

09:15:19

13 A No, I would not.

09:15:20

14 Q Have you done any consulting work that has
15 involved doing Suzuki reactions?

09:15:23

09:15:26

16 A You mean other than this case?

09:15:35

17 Q Correct.

09:15:37

18 A I don't recall ever having done any detailed
19 work. I may have recommended that people try a Suzuki
20 reaction on occasion. But I have -- I -- I do not
21 recall any time where I went deeply into the weeds of
22 the Suzuki reaction.

09:15:44

09:15:48

09:15:51

09:15:56

09:16:00

23 Q Do you have any experience at all in doing
24 Suzuki reactions?

09:16:03

09:16:06

25 A Myself personally, I have never run a Suzuki

09:16:07

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1 reaction.

09:16:10

2 Q Have you ever designed syntheses that
3 involved the Suzuki reaction for others to perform?

09:16:15

09:16:21

4 A I cannot unequivocally say no, but I cannot
5 recall having done that previously.

09:16:29

09:16:32

6 Q What -- strike that.

09:16:45

7 Would you describe your familiarity with
8 Suzuki reactions.

09:16:45

09:16:46

9 A Well, I -- prior to this case, I certainly
10 knew of them. They really began to come into
11 prominence, I would say, in the late 1990s, when they
12 became one of the new methods for making especially
13 biaryl compounds, which probably, prior to the
14 mid-'80,s had been a synthesis which was generally
15 considered difficult. And people tended to avoid
16 biaryls in drugs a great deal because there were not
17 good synthetic methods to make them.

09:16:48

09:16:52

09:16:57

09:17:02

09:17:09

09:17:14

09:17:17

09:17:21

09:17:25

18 And then several reactions, including the
19 Suzuki reaction, started to come into prominence, I'd
20 say, in the 1980s and the 1990s.

09:17:27

09:17:31

09:17:34

21 So I would be familiar with the idea that the
22 Suzuki reaction was a good reaction for making
23 biaryls.

09:17:37

09:17:41

09:17:47

24 Q And just to be clear, for those of us who
25 aren't chemists, a biaryl is an aryl-aryl bond; is

09:17:47

09:17:50

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1 THE VIDEOGRAPHER: We are now back on the 10:22:38
2 record. The time is 10:23. 10:22:41

3 MR. STEINDLER: Q. How did you come to be 10:22:43
4 engaged in this case? 10:22:45

5 A I was out working in my yard, and I got a 10:22:47
6 phone call from Denise Glassmeyer of Young Basile. 10:22:54
7 And that was my first intimation of this case. 10:23:00

8 Q How -- strike that. 10:23:06

9 What was your assignment? 10:23:07

10 A Well, I talked to the -- the lawyers at Young 10:23:17
11 Basile, and they explained to me what the case was 10:23:23
12 about. And initially, I obviously took a look at the 10:23:25
13 documentation and told them what I thought. 10:23:37

14 Q What were you asked to do? 10:23:38

15 A Initially, I think I -- I mean, I can't 10:23:48
16 recall exactly. But I think initially, I was asked to 10:23:52
17 take a look at the documentation and tell them what I 10:23:54
18 thought. 10:23:58

19 Q About what? 10:23:59

20 MR. SAMUELS: Objection; work product. 10:24:00

21 I instruct the witness to wait to answer 10:24:02
22 factual information about what was conveyed about the 10:24:04
23 nature of the assignment. 10:24:07

24 MR. STEINDLER: Well, I -- there is no 10:24:10
25 privilege between a testifying expert and any lawyers. 10:24:12

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1 So it may well be that I wrote it down early on, and 10:41:05
2 then used the literature to confirm it. 10:41:10

3 Or it may be that I wrote a slightly 10:41:13
4 different synthesis originally, and then, when I went 10:41:16
5 into the literature, decided that the one that we 10:41:19
6 ended up following was a better bet. 10:41:22

7 Q Did you actually run any reactions to try to 10:41:25
8 synthesize any of the steps in what ultimately 10:41:34
9 became -- strike that. 10:41:37

10 Did you run any reactions that are not 10:41:38
11 reported in your expert report? 10:41:40

12 A The -- there were, I think, 33 reactions run 10:41:47
13 in total. The expert report clearly reports on a 10:41:51
14 synthesis of the compound, and that in each case, 10:42:01
15 we'll use a particular example of a reaction. 10:42:04

16 And -- and rather obviously, if you're going 10:42:08
17 from A to B to C to D, you only will report reactions 10:42:11
18 which successfully carried out each of those steps. 10:42:16

19 Q Did you actually conduct reactions that did 10:42:19
20 not successfully carry out one or more of those steps? 10:42:24

21 A Yes. 10:42:27

22 Q Now, is that disclosed in your expert report? 10:42:27

23 A No, other than in the correction, where I 10:42:29
24 said that it was the third attempt at the Suzuki which 10:42:34
25 gave us the product on the road to dabrafenib. 10:42:38

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1 In fact, I think I probably -- if you read 10:42:46
2 the text, I probably -- for instance, I mentioned that 10:42:48
3 there were brominations which failed. 10:42:51

4 The -- so I would have to go back and read 10:42:53
5 exactly what I said there, because I -- I may well 10:42:59
6 have pointed out that some things didn't work. 10:43:05

7 So -- okay. So for instance, in the 10:43:16
8 bromination on page 23, this paragraph 54, I wrote 10:43:16
9 although the -- and this is line 4: 10:43:23

10 "Although the conditions described in some of 10:43:25
11 the literature proved to be impractically slow" -- 10:43:27

12 Which clearly means we tried some things 10:43:38
13 which proved to be impractically slow. Then I said 10:43:38
14 how we made it work. 10:43:41

15 When -- when you report out chemistry, it is 10:43:42
16 not customary to report out a whole lot of things 10:43:44
17 which don't work, because nobody on Earth cares how 10:43:46
18 not to make a compound, normally. 10:43:53

19 Q Just to be clear, you're only reporting in 10:44:00
20 your expert report what actually worked, and didn't 10:44:03
21 report in your expert report the things that did not 10:44:06
22 work; is that correct? 10:44:10

23 A That would be correct, certainly as far as 10:44:11
24 the experimentals are concerned. It is not in any way 10:44:13
25 professional practice to write up experimentals on 10:44:19

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1 reactions which did not work. 10:44:22

2 Q Okay. How long did it take you, from the 10:44:25
3 time that you wrote down your syntheses for Compounds 10:44:35
4 1 and 2, to actually complete successfully those 10:44:42
5 reactions? 10:44:50

6 A I would say the synthetic protocol was 10:44:51
7 probably first written out somewhere in around August 10:44:53
8 of last year. Maybe the one we actually used was 10:44:59
9 written up a couple of months later. I -- I don't 10:45:04
10 recall exactly. 10:45:06

11 And I think the final product was signed off 10:45:08
12 on in the lab notebook on -- on the 5th of March -- 10:45:13

13 Q Did you -- 10:45:18

14 A -- of this year. 10:45:20

15 Q -- did you modify your original synthetic 10:45:40
16 protocol to come up with the one that you actually 10:45:47
17 used? 10:45:50

18 A I think originally, we probably -- I -- I 10:45:54
19 probably -- well, I did first consider following the 10:45:58
20 same polarity of the Suzuki reaction as is described 10:46:08
21 in Scheme 2. 10:46:12

22 At -- upon further examination of the 10:46:17
23 literature, I felt there would be a higher probability 10:46:20
24 of success if we ran the Suzuki the other way around. 10:46:23

25 And I did not expect to be in a position 10:46:28

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1 where we would be able to spend a great deal of time 10:46:32
2 and resources looking at more than one route. 10:46:35

3 So at the end of the day, I had to go with 10:46:42
4 the route which, in my judgment, had the highest 10:46:44
5 probability of success. 10:46:47

6 Q How many different synthetic routes did you 10:46:48
7 consider for making Compound 2? 10:46:52

8 A Probably at least half a dozen pretty closely 10:47:00
9 related variants on the route, some of which I 10:47:06
10 probably discarded on the spot. 10:47:11

11 But this sort of coupling and, you know, the 10:47:14
12 fact, for instance, that the thiazole has two aryl -- 10:47:18
13 well, an aryl and a heteroaryl substituted on it, 10:47:24
14 means, for instance, I could have considered putting 10:47:30
15 on -- and I'm sure I did consider putting on the 10:47:32
16 pyrimidyl substituent using a Suzuki. But I chose to 10:47:37
17 use a Stille. 10:47:39

18 But I'm sure that all of these things were in 10:47:40
19 my routes at some point or another. 10:47:43

20 Q Did you do some experimentation with the 10:47:46
21 earlier iterations of your synthetic scheme that you 10:47:54
22 decided showed you that some of the steps didn't work? 10:47:57

23 A There was no experimentation done prior to 10:48:00
24 the execution of the scheme as was done by me. The -- 10:48:03
25 this -- by the time we decided -- by the time that 10:48:10

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1 Plexxikon actually had signed contracts to run this 10:48:17
2 synthesis, we were already at the end of last year. 10:48:23
3 So we had to run the one scheme and hoped that it 10:48:29
4 worked. 10:48:35

5 Q How many different synthetic schemes did you 10:48:39
6 put together for Compound 1? 10:48:48

7 A I would think one. 10:49:00

8 Q Do you know whether Adesis ever made any 10:49:03
9 other compounds for this case, aside from the two that 10:49:06
10 they made at your direction? 10:49:11

11 A I have no knowledge of anything that Adesis 10:49:18
12 does outside of the contract that I supervised for 10:49:21
13 Plexxikon/Durie Tangri/Young Basile. 10:49:28

14 So I know only of such reactions. I have no 10:49:38
15 idea whether there are any others. 10:49:42

16 Q Did you keep records of the reactions that 10:49:46
17 you did run or had run for you that were unsuccessful? 10:49:52

18 A I have the records of the reactions which 10:49:57
19 were run on the contract for Plexxikon. 10:50:04

20 Q They are not included in your expert report; 10:50:10
21 is that correct? 10:50:13

22 A My expert report does not include them, 10:50:15
23 because my expert report was how compounds are made, 10:50:17
24 not how they are not made. 10:50:21

25 Q In the various iterations of your synthetic 10:50:31

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1 due to the court by March 12th, we really didn't have 11:13:04
2 the time to explore further routes in any way. 11:13:07

3 Q When you said "the synthetic campaign at 11:13:13
4 Adesis," what did that include? 11:13:17

5 A That included all of the reactions shown in 11:13:19
6 my report. 11:13:24

7 Q It also included reactions not shown in your 11:13:25
8 report that were failed reactions; correct? 11:13:29

9 A They -- there were various com- -- sometimes 11:13:31
10 repeats of reactions which didn't work, then worked 11:13:36
11 when repeated. And on one or two occasions, we had to 11:13:39
12 change the conditions somewhat on the reactions. 11:13:43

13 Q How many people at Adesis were involved in 11:13:47
14 the synthetic campaign? 11:13:53

15 A There were two people at Adesis who were 11:13:55
16 directly involved in some fashion with the synthetic 11:14:00
17 campaign. 11:14:03

18 Q How long did it take them to make the 11:14:12
19 dabrafenib molecule following the synthetic scheme 11:14:16
20 that you gave them? 11:14:19

21 A Well, first of all, there were two people at 11:14:20
22 Adesis involved. One of them was purely involved in 11:14:25
23 the communication between myself and the chemist. 11:14:28

24 There was one bench chemist, Dr. Guan Lin 11:14:37
25 Bao, who worked, I would assume, 40 working days at 11:14:43

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1 the bench, minus perhaps a couple of public holidays. 11:14:48

2 So I would say probably 38 to 40 working days 11:14:53
3 were involved by one chemist. 11:14:59

4 Q And so just so I'm clear, 38 to 40 working 11:15:03
5 days were involved to make one compound; is that 11:15:06
6 right? 11:15:09

7 A No, to make two compounds -- well, to 11:15:09
8 complete the synthesis of two compounds. Obviously, 11:15:14
9 all the intermediates had to be made along the way. 11:15:16

10 Q Do you know how long it took Adesis to make 11:15:20
11 one of the compounds? 11:15:25

12 A I can give you the answer for Compound 1, I 11:15:33
13 think. Well, I'm -- I -- I can answer that question 11:15:33
14 if you get a little more particular. 11:15:38

15 Q Why don't you give me the answer that -- 11:15:43
16 that -- that you say you have. 11:15:45

17 A I believe that Compound 1 was -- the notebook 11:15:46
18 was signed, if I recall correctly, on the 12th of 11:15:50
19 January. And I think the synthetic campaign started 11:15:57
20 on the 5th of January. So that would presumably be 11:16:01
21 five working days. 11:16:04

22 Q And how about for Compound 2? How long did 11:16:09
23 that take? 11:16:11

24 A That was signed off, I think, on the 12th 11:16:12
25 of -- no, 5th of March. Sorry. 11:16:15

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CERTIFICATE OF REPORTER

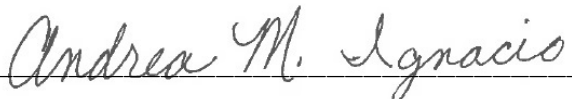
I, ANDREA M. IGNACIO, hereby certify that the witness in the foregoing deposition was by me duly sworn to tell the truth, the whole truth, and nothing but the truth in the within-entitled cause;

That said deposition was taken in shorthand by me, a disinterested person, at the time and place therein stated, and that the testimony of the said witness was thereafter reduced to typewriting, by computer, under my direction and supervision;

That before completion of the deposition, review of the transcript [] was [x] was not requested. If requested, any changes made by the deponent (and provided to the reporter) during the period allowed are appended hereto.

I further certify that I am not of counsel or attorney for either or any of the parties to the said deposition, nor in any way interested in the event of this cause, and that I am not related to any of the parties thereto.

Dated:



ANDREA M. IGNACIO, RPR, CRR, CCRR, CLR, CSR No. 9830